

Fig.1a-1

Nucleic acid and amino acid sequence of TTXi DRG sodium channel

```
tagcttgcttctgctaattgctaccccaggcctttagacagagaacagatggcagatggag
1 -----+-----+-----+-----+-----+-----+-----+
atcgaacgaagacgattacgatgggggtccggaaatctgtctcttgtctaccgtctacctc

tttcttattgccaatgcgcaaacgctgagccacctcatgatcccggaccccatgggttttc
61 -----+-----+-----+-----+-----+-----+-----+
aaagaataacggtacgcgtttgcgactcgggtggagtactagggcctgggggtacaaaag

agtagacaacctgggctaagaagagatctccgaccttatagagcagcaaagagtgtaaat
121 -----+-----+-----+-----+-----+-----+-----+
tcattctgttggaacccgattcttctcttagaggctggaatatctcgtcgtttctcacattta

tcttcccccaagaagaatgagaagATGGAGCTCCCCTTTGCGTCCGTGGGAACCTACCAATT
181 -----+-----+-----+-----+-----+-----+-----+
agaaggggttcttcttactcttctTACCTCGAGGGGAAACGCAGGCACCCTTGATGGTTAA

M E L P F A S V G T T N F

TCAGACGGTTCCTCCAGAGTCACTGGCAGAGATCGAGAAGCAGATTGCTGCTCACC GGG
241 -----+-----+-----+-----+-----+-----+-----+
AGTCTGCCAAGTGAGGTCTCAGTGACCGTCTCTAGCTCTTCGTCTAACGACGAGTG GCCC

R R F T P E S L A E I E K Q I A A H R A

CAGCCAAGAAGGCCAGAACCAAGCACAGAGGACAGGAGGACAAGGGCGAGAAGCCCAGGC
301 -----+-----+-----+-----+-----+-----+-----+
GTCGGTTCTTCCGGTCTTG GTTCGTGTCTCCTGTCTCCTGTTCCCGCTCTTCGGGTCCG

A K K A R T K H R G Q E D K G E K P R P

CTCAGCTGGACTTGAAAGACTGTAACCAGCTGCCCAAGTTCTATGGTGAGCTCCCAGCAG
361 -----+-----+-----+-----+-----+-----+-----+
GAGTCGACCTGAACTTTCTGACATTGGTCGACGGGTTCAGATACCACTCGAGGGTCTGTC

Q L D L K D C N Q L P K F Y G E L P A E

AACTGGTCGGGGAGCCCCCTGGAGGACCTAGACCCTTTCTACAGCACACACCGGACATTCA
421 -----+-----+-----+-----+-----+-----+-----+
TTGACCAGCCCCCTCGGGGACCTCCTGGATCTGGGAAAGATGTCGTGTGTGGCCTGTAAGT

L V G E P L E D L D P F Y S T H R T F M

TGGTGTGTAATAAAAGCAGGACCATTTCCAGATTCAAGTGCCACTTGGGCCCTGTGGCTCT
481 -----+-----+-----+-----+-----+-----+-----+
ACCACAACCTTATTTTCGTCCTGGTAAAGGTCTAAGTCACGGTGAACCCGGGACACCGAGA

V L N K S R T I S R F S A T W A L W L F
```

Fig.1a-2

TCAGTCCCTTCAACCTGATCAGAAGAACAGCCATCAAAGTGTCTGTCCATTCTGGTTCT
541 -----+-----+-----+-----+-----+-----+-----+
AGTCAGGGAAGTTGGACTAGTCTTCTTGTCTGGTAGTTTCACAGACAGGTAAGGACCAAGA
S P F N L I R R T A I K V S V H S W F S
CCATATTTCATCACCATCACTATTTTGGTCAACTGCGTGTGCATGACCCGAACTGATCTTC
601 -----+-----+-----+-----+-----+-----+-----+
GGTATAAGTAGTGGTAGTGATAAAACCAGTTGACGCACACGTAAGTGGGCTTGACTAGAAG
I F I T I T I L V N C V C M T R T D L P
CAGAGAAAGTCGAGTACGTCTTCACTGTCAATTTACACCTTCGAGGCTCTGATTAAGATAC
661 -----+-----+-----+-----+-----+-----+-----+
GTCTCTTTCAGCTCATGCAGAAGTGACAGTAAATGTGGAAGCTCCGAGACTAATTCTATG
E K V E Y V F T V I Y T F E A L I K I L
TGGCAAGAGGGTTTTGTCTAAATGAGTTCACTTATCTTCGAGATCCGTGGAAGTGGCTGG
721 -----+-----+-----+-----+-----+-----+-----+
ACCGTTCTCCCAAACAGATTTACTCAAGTGAATAGAAGCTCTAGGCACCTTGACCGACC
A R G F C L N E F T Y L R D P W N W L D
ACTTCAGTGTCAATTACCTTGGCGTATGTGGGTGCAGCGATAGACCTCCGAGGAATCTCAG
781 -----+-----+-----+-----+-----+-----+-----+
TGAAGTCACAGTAATGGAACCGCATAACCCACGTCGCTATCTGGAGGCTCCTTAGAGTC
F S V I T L A Y V G A A I D L R G I S G -
GCCTGCGGACATTCCGAGTTCTCAGAGCCCTGAAAAGTGTCTGTGATCCAGGACTGA
841 -----+-----+-----+-----+-----+-----+-----+
CGGACGCTGTAAAGGCTCAAGAGTCTCGGGACTTTTGACAAAGACACTAGGGTCTGACT
L R T F R V L R A L K T V S V I P G L K -
AGGTCATCGTGGGAGCCCTGATCCACTCAGTGAGGAAGCTGGCCGACGTGACTATCCTCA
901 -----+-----+-----+-----+-----+-----+-----+
TCCAGTAGCACCCCTCGGGACTAGGTGAGTCACTCCTTCGACCGGCTGCACTGATAGGAGT
V I V G A L I H S V R K L A D V T I L T
CAGTCTTCTGCCTGAGCGTCTTCGCCTTGGTGGGCCTGCAGCTCTTTAAGGGGAACCTTA
961 -----+-----+-----+-----+-----+-----+-----+
GTCAGAAGACGGACTCGCAGAAGCGGAACCAACCGGACGTCGAGAAATTCCCCTTGAAT
V F C L S V F A L V G L Q L F K G N L K
AGAACAAATGCATCAGGAACGGAACAGATCCCCACAAGGCTGACAACCTCTCATCTGAAA
1021 -----+-----+-----+-----+-----+-----+-----+
TCTTGTTTACGTAGTCCTTGCCTTGTCTAGGGGTGTTCCGACTGTTGGAGAGTAGACTTT
N K C I R N G T D P H K A D N L S S E M
TGGCAGAATACATCTTCATCAAGCCTGGTACTACGGATCCCTTACTGTGCGGCAATGGGT
1081 -----+-----+-----+-----+-----+-----+-----+
ACCGTCTTATGTAGAAGTAGTTCCGACCATGATGCCTAGGGAATGACACGCCGTTACCCA
A E Y I F I K P G T T D P L L C G N G S

Fig.1a-3

1141 CTGATGCTGGTCACTGCCCTGGAGGCTATGTCTGCCTGAAAACCTCCTGACAACCCGGATT
-----+-----+-----+-----+-----+-----+-----+
GACTACGACCAGTGACGGGACCTCCGATACAGACGGACTTTTGAGGACTGTTGGGCCTAA
D A G H C P G G Y V C L K T P D N P D F
1201 TTA ACTACACCAGCTTTGATTCTCTTTGCGTGGGCATTCTCTCACTGTTCCGCCTCATGA
-----+-----+-----+-----+-----+-----+-----+
AATTGATGTGGTCGAAACTAAGGAAACGCACCCGTAAGGAGAGTGACAAGGCGGAGTACT
N Y T S F D S F A W A F L S L F R L M T
1261 CGCAGGACTCCTGGGAGCGCCTGTACCAGCAGACACTCCGGGCTTCTGGGAAAATGTACA
-----+-----+-----+-----+-----+-----+-----+
GCGTCTTGAGGACCCTCGCGGACATGGTCGTCTGTGAGGCCCGAAGACCCTTTTACATGT
Q D S W E R L Y Q Q T L R A S G K M Y M
1321 TGGTCTTTTTTCGTGCTGGTTATTTTCCTTGATCGTTCTACCTGGTCAATTTGATCTTGG
-----+-----+-----+-----+-----+-----+-----+
ACCAGAAAAAGCACGACCAATAAAAGGAACCTAGCAAGATGGACCAGTTAACTAGAAC
V F F V L V I F L G S F Y L V N L I L A
1381 CCGTGGTCACCATGGCGTATGAAGAGCAGAGCCAGGCAACAATTGCAGAAATCGAAGCCA
-----+-----+-----+-----+-----+-----+-----+
GGCACCAGTGGTACCGCATACTTCTCGTCTCGGTCCGTTGTTAACGTCTTTAGCTTCGGT
V V T M A Y E E Q S Q A T I A E I E A K
1441 AGGAAAAAAAGTTCCAGGAAGCCCTTGAGGTGCTGCAGAAGGAACAGGAGGTGCTGGCAG
-----+-----+-----+-----+-----+-----+-----+
TCCTTTTTTTCAAGGTCTTCGGGAACCTCCACGACGTCTTCCTTGTCCTCCACGACCGTC
E K K F Q E A L E V L Q K E Q E V L A A
1501 CCCTGGGGATTGACACGACCTCGCTCCAGTCCCACAGTGGATCACCTTAGCCTCCAAAA
-----+-----+-----+-----+-----+-----+-----+
GGGACCCCTAACTGTGCTGGAGCGAGGTACGGGTGTCACCTAGTGGGAATCGGAGGTTTT
L G I D T T S L Q S H S G S P L A S K N
1561 ACGCCAATGAGAGAAGACCCAGGGTGAAATCAAGGGTGTGAGAGGGCTCCACGGATGACA
-----+-----+-----+-----+-----+-----+-----+
TGCGGTTACTCTCTTCTGGGTCCCACTTTAGTTCCACAGTCTCCCGAGGTGCCTACTGT
A N E R R P R V K S R V S E G S T D D N
1621 ACAGGTCACCCCAATCTGACCCTTACAACCAGCGCAGGATGTCTTTCCTAGGCCTGTCTT
-----+-----+-----+-----+-----+-----+-----+
TGTCCAGTGGGGTTAGACTGGGAATGTTGGTCGCGTCCTACAGAAAGGATCCGGACAGAA
R S P Q S D P Y N Q R R M S F L G L S S
1681 CAGGAAGACGCAGGGCTAGCCACGGCAGTGTGTTCCACTTCCGAGCGCCCAGCCAAGACA
-----+-----+-----+-----+-----+-----+-----+
GTCCTTCTGCGTCCCGATCGGTGCCGTACACAAGGTGAAGGCTCGCGGGTTCGGTTCTGT
G R R R A S H G S V F H F R A P S Q D I

Fig.1a-4

1741 TCTCATTTCCTGACGGGATCACCCCTGATGATGGGGTCTTTCACGGAGACCAGGAAAGCC
-----+-----+-----+-----+-----+-----+-----+-----+
AGAGTAAAGGACTGCCCTAGTGGGGACTACTACCCAGAAAGTGCCTCTGGTCCTTTTCGG
S F P D G I T P D D G V F H G D Q E S R
GTCGAGGTTCCATATTGCTGGGCAGGGGTGCTGGGCAGACAGGTCCACTCCCCAGGAGCC
1801 -----+-----+-----+-----+-----+-----+-----+-----+
CAGCTCCAAGGTATAACGACCCGTCCCCACGACCCGTCTGTCCAGGTGAGGGGTCTCTCG
R G S I L L G R G A G Q T G P L P R S P
CACTGCCTCAGTCCCCCAACCCTGGCCGTAGACATGGAGAAGAGGGACAGCTCGGAGTGC
1861 -----+-----+-----+-----+-----+-----+-----+-----+
GTGACGGAGTCAGGGGGTTGGGACCGGCATCTGTACCTCTTCTCCCTGTCGAGCCTCAG
L P Q S P N P G R R H G E E G Q L G V P
CCACTGGTGAGCTTACCGCTGGAGCGCCTGAAGGCCCGGCACTCGACACTACAGGGCAGA
1921 -----+-----+-----+-----+-----+-----+-----+-----+
GGTGACCACTCGAATGGCGACCTCGCGGACTTCCGGGCCGTGAGCTGTGATGTCCCGTCT
T G E L T A G A P E G P A L D T T G Q K
AGAGCTTCCTGTCTGCGGGCTACTTGAACGAACCTTTCCGAGCACAGAGGGCCATGAGCG
1981 -----+-----+-----+-----+-----+-----+-----+-----+
TCTCGAAGGACAGACGCCCGATGAACTTGCTTGGAAAGGCTCGTGTCTCCCGGTACTCG
S F L S A G Y L N E P F R A Q R A M S V
TTGTCAGTATCATGACTTCTGTCATTGAGGAGCTTGAAGAGTCTAAGCTGAAGTGCCAC
2041 -----+-----+-----+-----+-----+-----+-----+-----+
AACAGTCATAGTACTGAAGACAGTAACTCCTCGAACTTCTCAGATTCGACTTCACGGGTG
V S I M T S V I E E L E E S K L K C P P
CCTGCTTGATCAGCTTCGCTCAGAAGTATCTGATCTGGGAGTGCTGCCCCAAGTGGAGGA
2101 -----+-----+-----+-----+-----+-----+-----+-----+
GGACGAACTAGTCGAAGCGAGTCTTCATAGACTAGACCCTCACGACGGGGTTACCTCCT
C L I S F A Q K Y L I W E C C P K W R K
AGTTCAAGATGGCGCTGTTGAGCTGGTGACTGACCCCTTCGCAGAGCTTACCATCACCC
2161 -----+-----+-----+-----+-----+-----+-----+-----+
TCAAGTTCTACCGCGACAAGCTCGACCACTGACTGGGGAAGCGTCTCGAATGGTAGTGGG
F K M A L F E L V T D P F A E L T I T L
TCTGCATCGTGGTGAACACCGTCTTCATGGCCATGGAGCACTACCCCATGACCGATGCCT
2221 -----+-----+-----+-----+-----+-----+-----+-----+
AGACGTAGCACCCTTGTGGCAGAAGTACCGGTACCTCGTGATGGGGTACTGGCTACGGA
C I V V N T V F M A M E H Y P M T D A F
TCGATGCCATGCTTCAAGCCGGCAACATTGTCTTCACCGTGTTTTTCACAATGGAGATGG
2281 -----+-----+-----+-----+-----+-----+-----+-----+
AGCTACGGTACGAAGTTCGGCCGTTGTAACAGAAGTGGCACAAAAGTGTTACCTCTACC
D A M L Q A G N I V F T V F F T M E M A

Fig.1a-5

2341 CCTTCAAGATCATTGCCTTCGACCCCTACTATTACTTCCAGAAGAAGTGAATATCTTCG
-----+-----+-----+-----+-----+
GGAAGTTCTAGTAACGGAAGCTGGGGATGATAATGAAGGTCTTCTTCACCTTATAGAAGC
F K I I A F D P Y Y Y F Q K K W N I F D
2401 ACTGTGTCATCGTCACCGTGAGCCTTCTGGAGCTGAGTGCATCCAAGAAGGGCAGCCTGT
-----+-----+-----+-----+-----+
TGACACAGTAGCAGTGGCACTCGGAAGACCTCGACTCACGTAGGTTCTTCCCGTCGGACA
C V I V T V S L L E L S A S K K G S L S
2461 CTGTGCTCCGTTCTTACGCTTGCTGCGGGTCTTCAAGCTGGCCAAGTCCTGGCCCCACCC
-----+-----+-----+-----+-----+
GACACGAGGCAAGGAATGCGAACGACGCCCAGAAGTTCGACCGGTTTCAGGACCGGGTGGG
V L R S L R L L R V F K L A K S W P T L
2521 TGAACACCCTCATCAAGATCATCGGGAACCTCAGTGGGGGCCCTGGGCAACCTGACCTTTA
-----+-----+-----+-----+-----+
ACTTGTGGGAGTAGTTCTAGTAGCCCTTGAGTCACCCCGGGACCCGTTGGACTGGAAT
N T L I K I I G N S V G A L G N L T F I
2581 TCCTGGCCATCATCGTCTTCATCTTCGCCCTGGTTCGGAAAGCAGCTTCTCTCAGAGGACT
-----+-----+-----+-----+-----+
AGGACCGGTAGTAGCAGAAGTAGAAGCGGGACCAGCCTTTCGTCGAAGAGAGTCTCCTGA
L A I I V F I F A L V G K Q L L S E D Y
2641 ACGGGTGCCGCAAGGACGGCGTCTCCGTGTGGAACGGCGAGAAGCTCCGCTGGCACATGT
-----+-----+-----+-----+-----+
TGCCACGGCGTTCCTGCCGCAGAGGCACACCTTGCCGCTCTTCGAGGCGACCGTGTACA
G C R K D G V S V W N G E K L R W H M C
2701 GTGACTTCTTCCATTCCCTTCCTGGTCTTCCGAATCCTCTGCGGGGAGTGGATCGAGA
-----+-----+-----+-----+-----+
CACTGAAGAAGGTAAGGAAGGACCAGCAGAAGGCTTAGGAGACGCCCTCACCTAGCTCT
D F F H S F L V V F R I L C G E W I E N
2761 ACATGTGGGTCTGCATGGAGGTCAGCCAGAAATCCATCTGCCTCATCCTCTTCTTGACTG
-----+-----+-----+-----+-----+
TGTACACCCAGACGTACCTCCAGTCGGTCTTTAGGTAGACGGAGTAGGAGAAGAACTGAC
M W V C M E V S Q K S I C L I L F L T V
2821 TGATGGTGTCTGGGCAACCTAGTGGTGTCTCAACCTTTTCATCGCTTTACTGCTGAACTCCT
-----+-----+-----+-----+-----+
ACTACCACGACCCGTTGGATCACCACGAGTTGGAAGAGTAGCGAAATGACGACTTGAGGA
M V L G N L V V L N L F I A L L L N S F
2881 TCAGCGCGGACAACCTCACGGCTCCAGAGGATGACGGGGAGGTGAACAACTTGCAGTTAG
-----+-----+-----+-----+-----+
AGTCGCGCCTGTTGGAGTGCCGAGGTCTCCTACTGCCCTCCACTTGTTGAACGTCAATC
S A D N L T A P E D D G E V N N L Q L A

Fig.1a-6

2941 CACTGGCCAGGATCCAGGTA CTTGGCCATCGGGCCAGCAGGGCCATCGCCAGTTACATCA
-----+-----+-----+-----+-----+-----+-----+
GTGACCGGTCCTAGGTCCATGAACCGGTAGCCCGGTCTGTCCTCCGGTAGCGGTCAATGTAGT
L A R I Q V L G H R A S R A I A S Y I S
3001 GCAGCCACTGCCGATTCCGCTGGCCCAAGGTGGAGACCCAGCTGGGCATGAAGCCCCAC
-----+-----+-----+-----+-----+-----+-----+
CGTCGGTGACGGCTAAGGCGACCGGGTTCCACCTCTGGGTCTGACCCGTACTTCGGGGGGTG
S H C R F R W P K V E T Q L G M K P P L
3061 TCACCAGCTCAGAGGCCAAGAACCACATTGCCACTGATGCTGTCAGTGTGTCAGTGGGGA
-----+-----+-----+-----+-----+-----+-----+
AGTGGTCTGAGTCTCCGGTTCTTGGTGTAACGGTGACTACGACAGTCACGACGTCACCCCT
T S S E A K N H I A T D A V S A A V G N
3121 ACCTGACAAAGCCAGCTCTCAGTAGCCCCAAGGAGAATCACGGGGACTTCATCACTGATC
-----+-----+-----+-----+-----+-----+-----+
TGGACTGTTTCGGTCTGAGAGTCATCGGGGTTCTCTTAGTGCCCCTGAAGTAGTGACTAG
L T K P A L S S P K E N H G D F I T D P
3181 CCAACGTGTGGGTCTCTGTGCCCATTTGCTGAGGGGGAATCTGACCTCGACGAGCTCGAGG
-----+-----+-----+-----+-----+-----+-----+
GGTTGCACACCCAGAGACACGGGTAACGACTCCCCCTTAGACTGGAGCTGCTCGAGCTCC
N V W V S V P I A E G E S D L D E L E E
3241 AAGATATGGAGCAGGCTTCGCAGAGCTCCTGGCAGGAAGAGGACCCCAAGGGACAGCAGG
-----+-----+-----+-----+-----+-----+-----+
TTCTATACCTCGTCCGAAGCGTCTCGAGGACCGTCTTCTCCTGGGGTTCCCTGTCTGCTCC
D M E Q A S Q S S W Q E E D P K G Q Q E
3301 AGCAGTTGCCACAAGTCCAAAAGTGTGAAAACCACCAGGCAGCCAGAAGCCCAGCCTCCA
-----+-----+-----+-----+-----+-----+-----+
TCGTCAACGGTGTTTCAGGTTTTACACTTTTGGTGGTCCGTCGGTCTTCGGGTCTGGAGGT
Q L P Q V Q K C E N H Q A A R S P A S M
3361 TGATGTCCTCTGAGGACCTGGCTCCATACCTGGGTGAGAGCTGGAAGAGGAAGGATAGCC
-----+-----+-----+-----+-----+-----+-----+
ACTACAGGAGACTCCTGGACCGAGGTATGGACCCACTCTCGACCTTCTCCTTCCTATCGG
M S S E D L A P Y L G E S W K R K D S P
3421 CTCAGGTCCCTGCCGAGGGAGTGGATGACACGAGCTCCTCTGAGGGCAGCACGGTGGACT
-----+-----+-----+-----+-----+-----+-----+
GAGTCCAGGGACGGCTCCCTCACCTACTGTGCTCGAGGAGACTCCCGTCTGTCACCTGA
Q V P A E G V D D T S S S E G S T V D C
3481 GCCCGGACCCAGAGGAAATCCTGAGGAAGATCCCCGAGCTGGCAGATGACCTGGACGAGC
-----+-----+-----+-----+-----+-----+-----+
CGGGCCTGGGTCTCCTTTAGGACTCCTTCTAGGGGCTCGACCGTCTACTGGACCTGCTCG
P D P E E I L R K I P E L A D D L D E P

Fig. 1a-7

3541 CCGATGACTGTTTCACAGAAGGCTGCACTCGCCGCTGTCCCTGCTGCAACGTGAATACTA
-----+-----+-----+-----+-----+-----+-----+
GGCTACTGACAAAGTGTCTTCCGACGTGAGCGGCGACAGGGACGACGTTGCACTTATGAT
D D C F T E G C T R R C P C C N V N T S
GCAAGTCTCCTTGGGCCACAGGCTGGCAGGTGCGCAAGACCTGCTACCGCATCGTGGAGC
3601 -----+-----+-----+-----+-----+-----+-----+
CGTTCAGAGGAACCCGGTGTCCGACCGTCCACGCGTTCTGGACGATGGCGTAGCACCTCG
K S P W A T G W Q V R K T C Y R I V E H
ACAGCTGGTTTGAGAGTTTCATCATCTTCATGATCCTGCTCAGCAGTGGAGCGCTGGCCT
3661 -----+-----+-----+-----+-----+-----+-----+
TGTCGACCAAACCTCTCAAAGTAGTAGAAGTACTAGGACGAGTCGTCACCTCGCGACCGGA
S W F E S F I I F M I L L S S G A L A F
TTGAGGATAACTACCTGGAAGAGAAACCCCGAGTGAAGTCCGTGCTGGAGTACACTGACC
3721 -----+-----+-----+-----+-----+-----+-----+
AACTCCTATTGATGGACCTTCTCTTTGGGGCTCACTTCAGGCACGACCTCATGTGACTGG
E D N Y L E E K P R V K S V L E Y T D R
GAGTGTTACCTTCATCTTCGTCTTTGAGATGCTGCTCAAGTGGGTAGCCTATGGCTTCA
3781 -----+-----+-----+-----+-----+-----+-----+
CTCACAAGTGAAGTAGAAGCAGAACTCTACGACGAGTTCACCCATCGGATACCGAAGT
V F T F I F V F E M L L K W V A Y G F K
AAAAGTATTTACCAATGCCTGGTGCTGGCTGGACTTCCTCATTTGTGAACATCTCCCTGA
3841 -----+-----+-----+-----+-----+-----+-----+
TTTTCATAAAGTGGTTACGGACCACGACCGACCTGAAGGAGTAACACTTGTAGAGGGACT
K Y F T N A W C W L D F L I V N I S L T
CAAGCCTCATAGCGAAGATCCTTGAGTATTCCGACGTGGCGTCCATCAAAGCCCTTCGGA
3901 -----+-----+-----+-----+-----+-----+-----+
GTTCCGAGTATCGCTTCTAGGAACTCATAAGGCTGCACCGCAGGTAGTTTCGGGAAGCCT
S L I A K I L E Y S D V A S I K A L R T
CTCTCCGTGCCCTCCGACCGCTGCGGGCTCTGTCTCGATTCTGAAGGCATGAGGGTAGTGG
3961 -----+-----+-----+-----+-----+-----+-----+
GAGAGGCACGGGAGGCTGGCGACGCCCCGAGACAGAGCTAAGCTTCCGTACTCCCATCACC
L R A L R P L R A L S R F E G M R V V V
TGGATGCCCTCGTGGGCGCCATCCCCCTCCATCATGAACGTCCTCCTCGTCTGCCTCATCT
4021 -----+-----+-----+-----+-----+-----+-----+
ACCTACGGGAGCACCCGCGGTAGGGGAGGTAGTACTTGCAGGAGGAGCAGACGGAGTAGA
D A L V G A I P S I M N V L L V C L I F
TCTGGCTCATCTTCAGCATCATGGGCGTGAACCTCTTCGCCGGGAAATTTTCGAAGTGCG
4081 -----+-----+-----+-----+-----+-----+-----+
AGACCGAGTAGAAGTCGTAGTACCCGCACTTGAGAGAAGCGGCCCTTTAAAGCTTCACGC
W L I F S I M G V N L F A G K F S K C V

Fig. 1a-8

4141 TCGACACCAGAAATAACCCATTTTCCAACGTGAATTCGACGATGGTGAATAACAAGTCCG
-----+-----+-----+-----+-----+-----+-----+
AGCTGTGGTCTTTATTGGGTAAAAGGTTGCACTTAAGCTGCTACCACTTATTGTTTCAGGC
D T R N N P F S N V N S T M V N N K S E
AGTGTCAACAATCAAAACAGCACCGGCCACTTCTTCTGGGTCAACGTCAAAGTCAACTTCG
4201 -----+-----+-----+-----+-----+-----+-----+
TCACAGTGTTAGTTTTGTCTGCGGCCGGTGAAGAAGACCCAGTTGCAGTTTCAGTTGAAGC
C H N Q N S T G H F F W V N V K V N F D
ACAACGTCGCTATGGGCTACCTCGCACTTCTTCAGGTGGCAACCTTCAAAGGCTGGATGG
4261 -----+-----+-----+-----+-----+-----+-----+
TGTTGCAGCGATACCCGATGGAGCGTGAAGAAGTCCACCGTTGGAAGTTTCCGACCTACC
N V A M G Y L A L L Q V A T F K G W M D
ACATAATGTATGCAGCTGTTGATTCCGGAGAGATCAACAGTCAGCCTAACTGGGAGAACA
4321 -----+-----+-----+-----+-----+-----+-----+
TGTATTACATACGTCGACAACCTAAGGCCTCTCTAGTTGTCAGTCGGATTGACCCCTCTGT
I M Y A A V D S G E I N S Q P N W E N N
ACTTGTACATGTACCTGTACTTCGTCTGTTTTTCATCATTTTTCGGTGGCTTCTTCACGCTGA
4381 -----+-----+-----+-----+-----+-----+-----+
TGAACATGTACATGGACATGAAGCAGCAAAAGTAGTAAAAGCCACCGAAGAAGTGCAGCT
L Y M Y L Y F V V F I I F G G F F T L N
ATCTCTTTGTTGGGGTCATAATCGACAACCTTCAACCAACAGAAAAAAAGCTAGGAGGCC
4441 -----+-----+-----+-----+-----+-----+-----+
TAGAGAAACAACCCAGTATTAGCTGTTGAAGTTGGTTGTCTTTTTTTTCGATCCTCCGG
L F V G V I I D N F N Q Q K K K L G G Q
AGGACATCTTCATGACAGAAGAGCAGAAGAAGTACTACAATGCCATGAAGAAGCTGGGCT
4501 -----+-----+-----+-----+-----+-----+-----+
TCCTGTAGAAGTACTGTCTTCTCGTCTTCTTCATGATGTTACGGTACTTCTTCGACCCGA
D I F M T E E Q K K Y Y N A M K K L G S
CCAAGAAACCCAGAACCCCATCCACGGCCCCTGAATAAGTACCAAGGCTTCGTGTTTG
4561 -----+-----+-----+-----+-----+-----+-----+
GGTTCTTTGGGGTCTTCGGGTAGGGTGCCGGGGACTTATTCATGGTTCCGAAGCACAAC
K K P Q K P I P R P L N K Y Q G F V F D
ACATCGTGACCAGGCAAGCCTTTGACATCATCATGTTCTCATCTGCCTCAACATGA
4621 -----+-----+-----+-----+-----+-----+-----+
TGTAGCACTGGTCCGTTTCGGAACCTGTAGTAGTAGTACCAAGAGTAGACGGAGTTGTACT
I V T R Q A F D I I I M V L I C L N M I
TCACCATGATGGTGGAGACCGACGAGCAGGGCGAGGAGAAGACGAAGGTTCTGGGCAGAA
4681 -----+-----+-----+-----+-----+-----+-----+
AGTGGTACTACCACCTCTGGCTGCTCGTCCCGCTCCTCTTCTGCTTCCAAGACCCGTCTT
T M M V E T D E Q G E E K T K V L G R I

Fig. 1a-9

4741 TCAACCAGTTCTTTGTGGCCGTCTTCACGGGCGAGTGTGTGATGAAGATGTTCCGCCCTGC
-----+-----+-----+-----+-----+-----+-----+
AGTTGGTCAAGAAACACCGGCAGAAGTGCCCGCTCACACACTACTTCTACAAGCGGGACG
N Q F F V A V F T G E C V M K M F A L R
GACAGTACTACTTCACCAACGGCTGGAACGTGTTTCGACTTCATAGTGGTGATCCTGTCCA
4801 -----+-----+-----+-----+-----+-----+-----+
CTGTCATGATGAAGTGGTTGCCGACCTTGACACAAGCTGAAGTATCACCACCTAGGACAGGT
Q Y Y F T N G W N V F D F I V V I L S I
TTGGGAGTCTGCTGTTTCTGCAATCCTTAAGTCACTGGAAAACACTTCTCCCCGACGC
4861 -----+-----+-----+-----+-----+-----+-----+
AACCCTCAGACGACAAAAGACGTTAGGAATTCAGTGACCTTTTGATGAAGAGGGGCTGCG
G S L L F S A I L K S L E N Y F S P T L
TCTTCCGGGTCATCCGTCTGGCCAGGATCGGCCGCATCCTCAGGCTGATCCGAGCAGCCA
4921 -----+-----+-----+-----+-----+-----+-----+
AGAAGGCCCAAGTAGGCAGACCGGTCCTAGCCGGCGTAGGAGTCCGACTAGGCTCGTCGGT
F R V I R L A R I G R I L R L I R A A K
AGGGGATTCGCACGCTGCTCTTCGCCCTCATGATGTCCCTGCCCCGCCCTCTTCAACATCG
4981 -----+-----+-----+-----+-----+-----+-----+
TCCCCTAAGCGTGCGACGAGAAGCGGGAGTACTACAGGGACGGGCGGGAGAAGTTGTAGC
G I R T L L F A L M M S L P A L F N I G
GCCTCCTCCTCTTCCTCGTCATGTTTCATCTACTCCATCTTCGGCATGGCCAGCTTCGCTA
5041 -----+-----+-----+-----+-----+-----+-----+
CGGAGGAGGAGAAGGAGCAGTACAAGTAGATGAGGTAGAAGCCGTACCGGTCTGAAGCGAT
L L L F L V M F I Y S I F G M A S F A N
ACGTCGTGGACGAGGCCGGCATCGACGACATGTTCAACTTCAAGACCTTTGGCAACAGCA
5101 -----+-----+-----+-----+-----+-----+-----+
TGCAGCACCTGCTCCGGCCGTAGCTGCTGTACAAGTTGAAGTTCTGGAACCGTTGTCGT
V V D E A G I D D M F N F K T F G N S M
TGCTGTGCCTGTTCCAGATCACCACCTCGGCCGGCTGGGACGGCCTCCTCAGCCCCATCC
5161 -----+-----+-----+-----+-----+-----+-----+
ACGACACGGACAAGGTCTAGTGGTGGAGCCGGCCGACCCTGCCGGAGGAGTCGGGGTAGG
L C L F Q I T T S A G W D G L L S P I L
TCAACACGGGGGCTCCCTACTGCGACCCCAACCTGCCCAACAGCAACGGCTCCCCGGGGGA
5221 -----+-----+-----+-----+-----+-----+-----+
AGTTGTGCCCCGGAGGGATGACGCTGGGGTTGGACGGGTGTCTGTTGCCGAGGGCCCCCT
N T G P P Y C D P N L P N S N G S R G N
ACTGCGGGAGCCCCGGCGGTGGGCATCATCTTCTTACCACCTACATCATCATCTCCTTCC
5281 -----+-----+-----+-----+-----+-----+-----+
TGACGCCCTCGGGCCGCCACCCGTAGTAGAAGAAGTGGTGGATGTAGTAGTAGAGGAAGG
C G S P A V G I I F F T T Y I I I S F L

Fig. 1a-10

5341 TCATCGTGGTCAACATGTACATCGCAGTGATTCTGGAGAACTTCAACGTAGCCACCGAGG
-----+-----+-----+-----+-----+-----+-----+-----+
AGTAGCACCAGTTGTACATGTAGCGTCACTAAGACCTCTTGAAGTTGCATCGGTGGCTCC
I V V N M Y I A V I L E N F N V A T E E
AGAGCACGGAGCCCCCTGAGCGAGGACGACTTCGACATGTTCTATGAGACCTGGGAGAAGT
5401 -----+-----+-----+-----+-----+-----+-----+-----+
TCTCGTGCCTCGGGGACTCGCTCCTGCTGAAGCTGTACAAGATACTCTGGACCCTCTTCA
S T E P L S E D D F D M F Y E T W E K F
TCGACCCGGAGGCCACCCAGTTCATTGCCTTTTCTGCCCTCTCAGACTTCGCGGACACGC
5461 -----+-----+-----+-----+-----+-----+-----+-----+
AGCTGGGCCTCCGGTGGGTCAAGTAACGGAAAGACGGGAGAGTCTGAAGCGCCTGTGCG
D P E A T Q F I A F S A L S D F A D T L
TCTCCGGCCCTCTTAGAATCCCCAAACCCAAACCAGAATATATTAATCCAGATGGACCTGC
5521 -----+-----+-----+-----+-----+-----+-----+-----+
AGAGGCCGGGAGAATCTTAGGGGTTTGGGTTGGTCTTATATAATTAGGTCTACCTGGACG
S G P L R I P K P N Q N I L I Q M D L P
CGTTGGTCCCCGGGGATAAGATCCACTGTCTGGACATCCTTTTTGCCTTCACAAAGAACG
5581 -----+-----+-----+-----+-----+-----+-----+-----+
GCAACCAGGGGCCCTATTCTAGGTGACAGACCTGTAGGAAAAACGGAAGTGTTCCTTGC
L V P G D K I H C L D I L F A F T K N V
TCTTGGGAGAATCCGGGGAGTTGGACTCCCTGAAGACCAATATGGAAGAGAAGTTTATGG
5641 -----+-----+-----+-----+-----+-----+-----+-----+
AGAACCCTCTTAGGCCCTCAACCTGAGGGACTTCTGGTTATACCTTCTCTTCAAATACC
L G E S G E L D S L K T N M E E K F M A
CGACCAATCTCTCCAAAGCATCCTATGAACCAATAGCCACCACCCTCCGGTGGAGCAGG
5701 -----+-----+-----+-----+-----+-----+-----+-----+
GCTGGTTAGAGAGGTTTCGTAGGATACTTGGTTATCGGTGGTGGGAGGCCACCTTCGTCC
T N L S K A S Y E P I A T T L R W K Q E
AAGACCTCTCAGCCACAGTCATTCAAAGGCCTACCGGAGCTACATGCTGCACCGCTCCT
5761 -----+-----+-----+-----+-----+-----+-----+-----+
TTCTGGAGAGTCGGTGTCAAGTMTTCCGGATGGCCTCGATGTACGACGTGGCGAGGA
D L S A T V I Q K A Y R S Y M L H R S L
TGACACTCTCCAACACCCTGCATGTGCCCAGGGCTGAGGAGGATGGCGTGTCACTTCCCG
5821 -----+-----+-----+-----+-----+-----+-----+-----+
ACTGTGAGAGGTTGTGGGACGTACACGGGTCCCGACTCCTCCTACCGCACAGTGAAGGGC
T L S N T L H V P R A E E D G V S L P G
GGGAAGGCTACAGTACATTCATGGCAAACAGTGGACTCCCGGACAAATCAGAACTGCCT
5881 -----+-----+-----+-----+-----+-----+-----+-----+
CCCTTCCGATGTCATGTAAGTACCGTTTGTCACTGAGGGCCTGTTAGTCTTTGACGGA
E G Y S T F M A N S G L P D K S E T A S

Fig. 1a-11

5941 CTGCTACGTCTTTCCCGCCATCCTATGACAGTGTACCAGGGGCCTGAGTGACCGGGCCA
-----+-----+-----+-----+-----+-----+
GACGATGCAGAAAGGGCGGTAGGATACTGTACAGTGGTCCCCGGACTCACTGGCCCCGGT

A T S F P P S Y D S V T R G L S D R A N

6001 ACATTAACCCATCTAGCTCAATGCAAAATGAAGATGAGGTCGCTGCTAAGGAAGGAAACA
-----+-----+-----+-----+-----+-----+
TGTAATTGGGTAGATCGAGTTACGTTTTACTTCTACTCCAGCGACGATTCCTTCCTTTGT

I N P S S S M Q N E D E V A A K E G N S

6061 GCCCTGGACCTCAGTGAaggcactcaggcatgcacagggcaggttccaatgtctttctct
-----+-----+-----+-----+-----+-----+
CGGGACCTGGAGTCACTtccgtgagtcggtacgtgtcccgtccaaggttacagaaagaga

P G P Q *

6121 gctgtactaactccttccctctgagggtggcaccaacctccagcctccaccaatgcatgt
-----+-----+-----+-----+-----+-----+
cgacatgattgaggaagggagacctccaccgtggttggagggtcggagggtggttacgtaca

6181 cactgggtcatggtgtcagaactgaatggggacatccttgagaaagccccaccccaatag
-----+-----+-----+-----+-----+-----+
gtgaccagtaccacagtcttgacttaccctgttaggaactctttcgggggtgggggttatc

6241 gaatcaaaagccaaggatactcctccattctgacgtcccttccgagttcccagaagatgt
-----+-----+-----+-----+-----+-----+
cttagttttcggttcctatgaggaggtaagactgcaggggaagggtcaagggtcttctaca

6301 cattgtcccttctgtttgtgaccagagacgtgattcaccaacttctcggagccagagac
-----+-----+-----+-----+-----+-----+
gtaacgaggggaagacaaacactgggtctctgcactaagtgggttgaagagcctcggtctctg

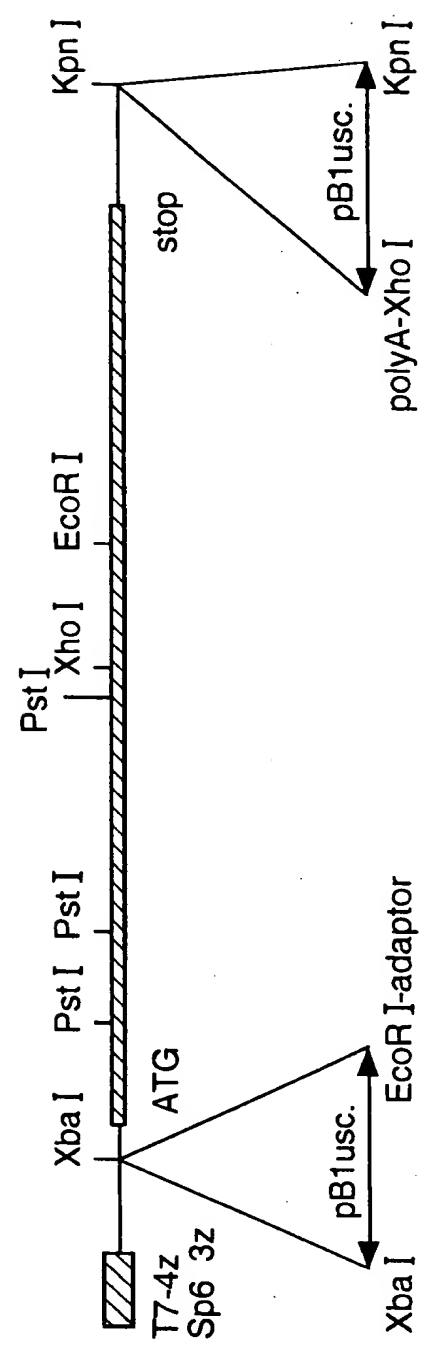
6361 acatagcaaagacttttctgctgggtgtcgggcagtcttagagaagtcacgtaggggttgg
-----+-----+-----+-----+-----+-----+
tgtatcgtttctgaaaagacgaccacagccgctcagaatctcttcagtgcaccccaacc

6421 tactgagaattagggtttgcattgactgcattgctcacagctgccggacaataacctgtgagt
-----+-----+-----+-----+-----+-----+
atgactcttaatcccaaacgtactgacgtacgagtggtcgacggcctgttatggacactca

6481 cggccattaaaattaatatttttaaagttaaaaaaaaaaaaaaaaa
-----+-----+-----+-----+-----+-----+
gccggtaatTTTaatataaaaaatttcaattttttttttttttt

Fig.1b

SNS-B voltage gated sodium channel
 PNC IB XOI-construct



Constructs were generated in pGem 3z
 and pGem 4z with bluescript polylinkers
 Linearisation site is KPN I

Fig.1c

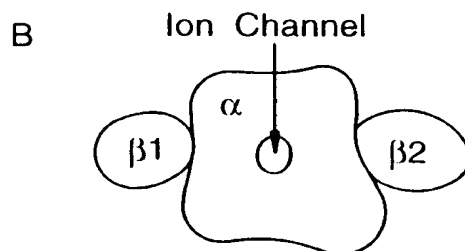
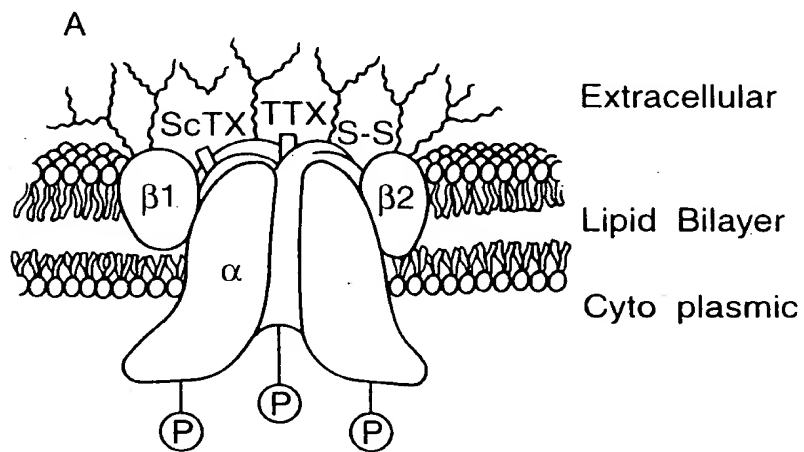
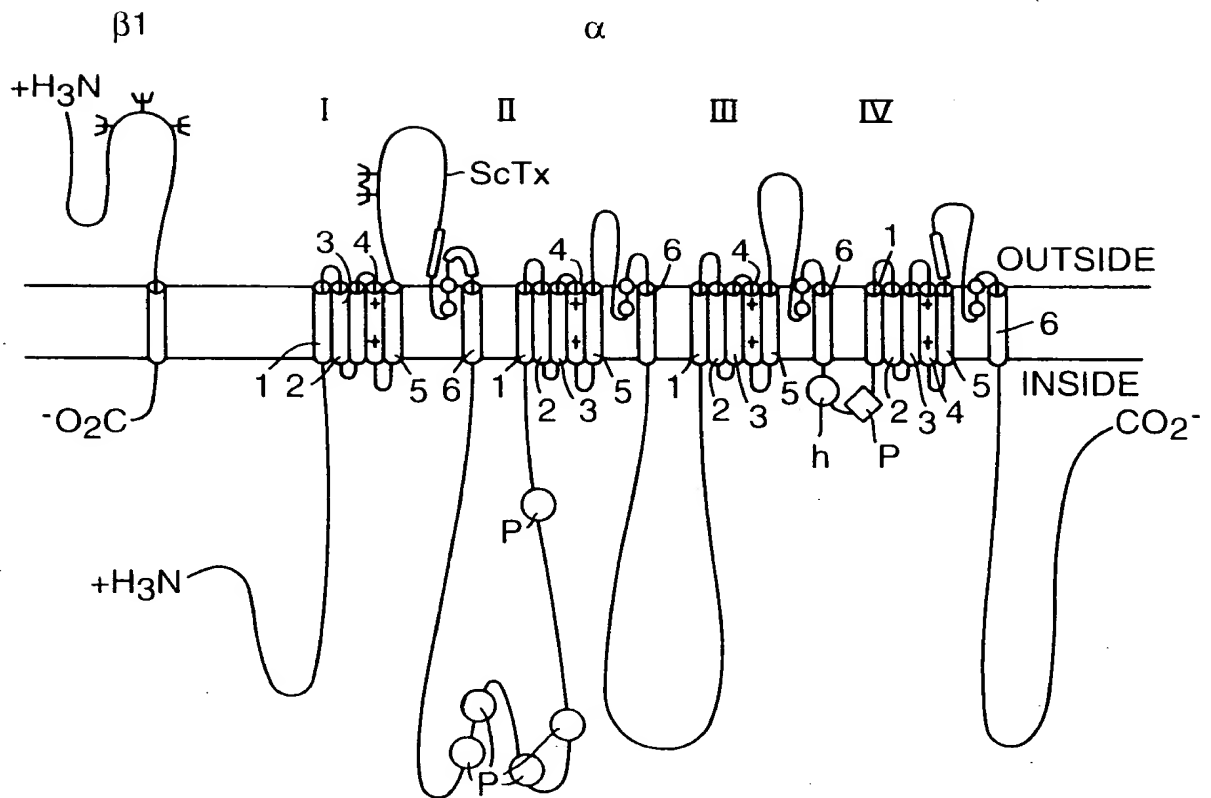


Fig.2

Sequence of PCR primers for isolation of human clone probes

a) *Highly conserved regions of all sodium channels*

1) Position 2475-2510 S4 Domain II

Degenerate primers (20-24mers) encoding amino acid residues RLLRVFKLAKSWPTL or non degenerate primers within this region e.g. 5' gcttgctgcgggtcttcaagc 3'

2) Position 3961 - 4010 S4 Domain III

Degenerate primers encoding the complementary strand encoding residues LRALPLRALS RFEG or non degenerate primers within this region e.g. 5' atcgagacagagcccgagcg 3'

b) *Unique sequence primers for SNS-homologues*

e.g. residues with the region 2641-2680

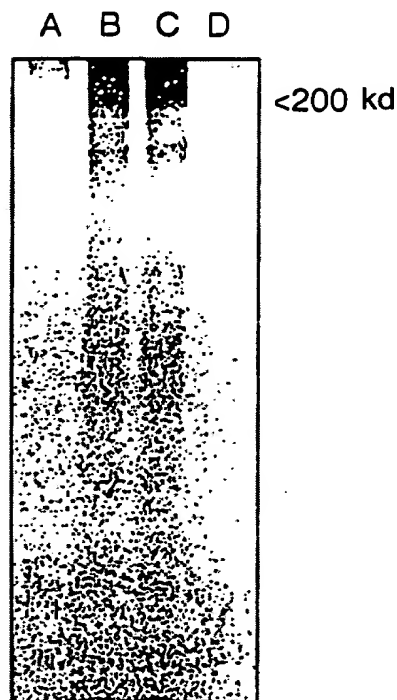
e.g. 5' acgggtgccgcaaggacggcggtctccgtgtggaacggcgagaag 3'

and complementary sequence within the region 3375 and 3420

e.g. 5' ggctatccttctcttccagctctcaccaggtatggagccaggt 3'

Fig.3

In vitro synthesis of S-35 methionine labelled SNS-B voltage gated sodium channel in a coupled transcription/translation system



Autoradiograph of a 7.5% SDS polyacrylamide gel, showing the migration of labelled proteins compared to the sizes of known molecular weight markers (Amersham rainbow markers). Lane A control, Lane B SNS-B, Lane C SNS-B, Lane D control. The predicted 200kDa band representing the SNS-B sodium channel is arrowed.

Fig.4a

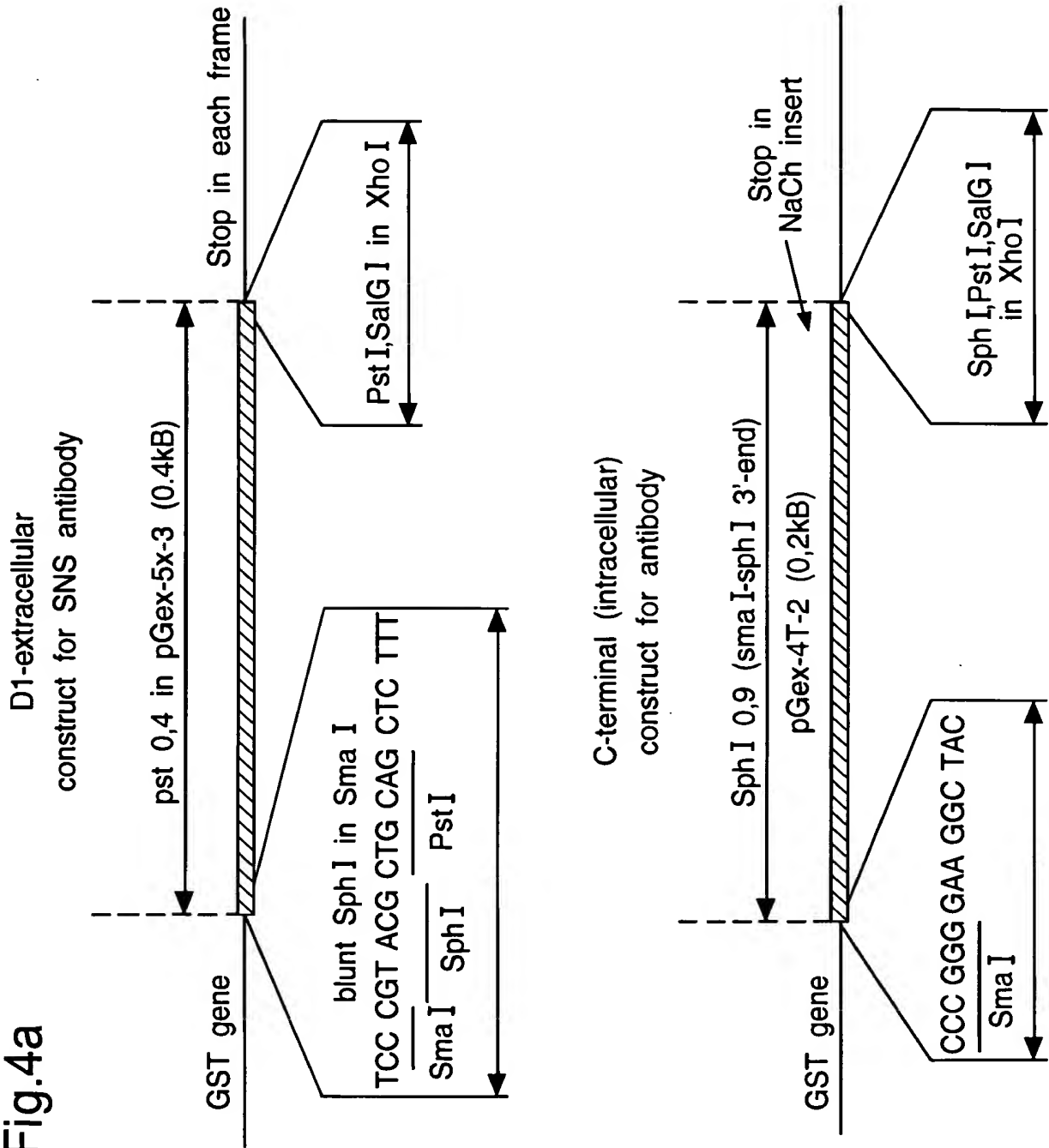


Fig.4b

